



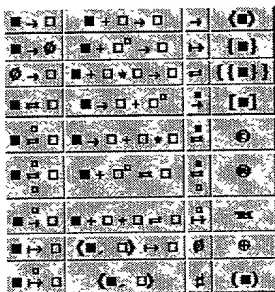
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California Institute of Technology

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▼ Reactions



▼ Cascades



► Functions

► Hill Function Options

▷ GRN Options

▶ NHCA Options

▷ **run Options**

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FIG. 1

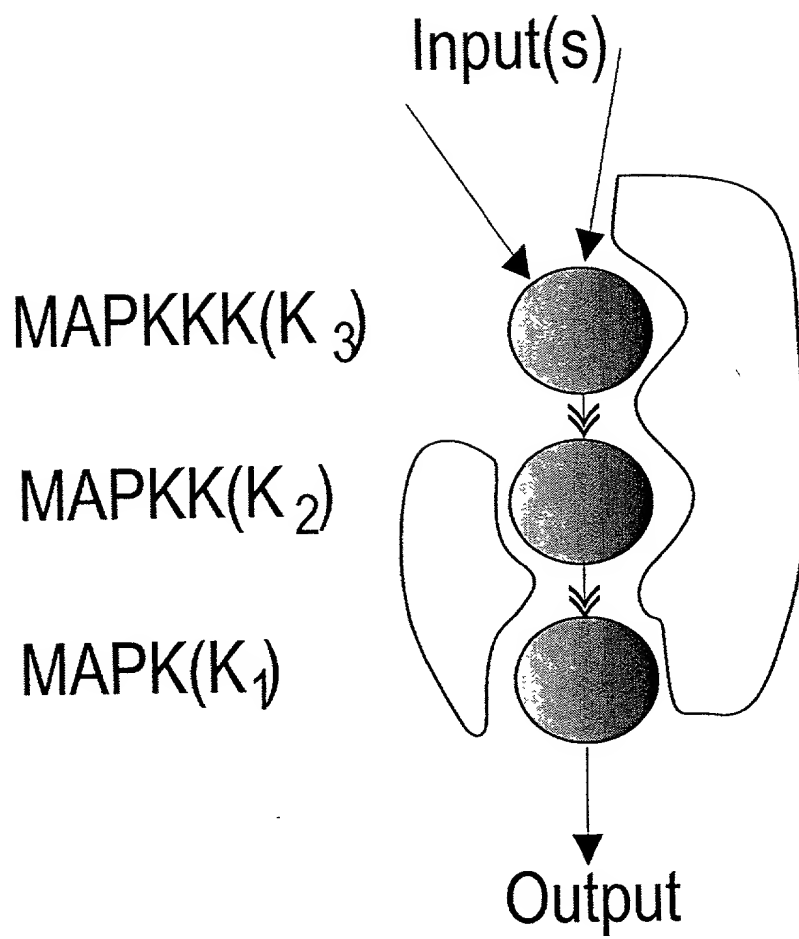


FIG. 2

```

      PFKA
r = {[ATP ⇌ ADP, k1, km1, k2],
     {∅ → ATP, v1},
     {ADP → ∅, v2},
     {PFK + ADP2 ⇌ PFKA, k3, km3}};
interpret[r]

```

```

{[ADP'[t] == -v2 ADP[t] + k2 ATP_PFKA[t] -
  k3 ADP[t]2 PFK[t] + km3 PFKA[t],
 ATP'[t] == v1 + km1 ATP_PFKA[t] -
  k1 ATP[t] PFKA[t],
 ATP_PFKA'[t] == -k2 ATP_PFKA[t] -
  km1 ATP_PFKA[t] + k1 ATP[t] PFKA[t],
 PFK'[t] == -k3 ADP[t]2 PFK[t] + km3 PFKA[t],
 PFKA'[t] == k2 ATP_PFKA[t] +
  km1 ATP_PFKA[t] + k3 ADP[t]2 PFK[t] -
  km3 PFKA[t] - k1 ATP[t] PFKA[t]},
 {ADP, ATP, ATP_PFKA, PFK, PFKA}]

```

FIG. 3

Variable	Mean	SD	Min	Max
Age	35.2	12.5	18	65
Gender	0.45	0.50	0	1
Marital Status	0.60	0.49	0	1
Education	12.5	2.5	9	16
Income	3500	1500	1000	8000
Health Status	0.70	0.46	0	1
Smoking	0.30	0.46	0	1
Alcohol	0.20	0.40	0	1
Exercise	0.10	0.30	0	1
Stress	4.5	1.5	1	7
Sleep	6.0	1.0	4	8
Appetite	5.5	1.0	3	7
Mood	4.0	1.0	2	6
Energy	5.0	1.0	3	7
Concentration	4.5	1.0	2	6
Memory	4.0	1.0	2	6
Emotion	4.5	1.0	2	6
Behavior	4.0	1.0	2	6
Thought	4.5	1.0	2	6
Feeling	4.0	1.0	2	6
Perception	4.5	1.0	2	6
Attention	4.0	1.0	2	6
Intuition	4.5	1.0	2	6
Imagination	4.0	1.0	2	6
Reasoning	4.5	1.0	2	6
Logic	4.0	1.0	2	6
Analysis	4.5	1.0	2	6
Synthesis	4.0	1.0	2	6
Evaluation	4.5	1.0	2	6
Comparison	4.0	1.0	2	6
Classification	4.5	1.0	2	6
Organization	4.0	1.0	2	6
Planning	4.5	1.0	2	6
Problem Solving	4.0	1.0	2	6
Decision Making	4.5	1.0	2	6
Communication	4.0	1.0	2	6
Interpersonal	4.5	1.0	2	6
Group	4.0	1.0	2	6
Team	4.5	1.0	2	6
Leadership	4.0	1.0	2	6
Management	4.5	1.0	2	6
Organization	4.0	1.0	2	6
Planning	4.5	1.0	2	6
Problem Solving	4.0	1.0	2	6
Decision Making	4.5	1.0	2	6
Communication	4.0	1.0	2	6
Interpersonal	4.5	1.0	2	6
Group	4.0	1.0	2	6
Team	4.5	1.0	2	6
Leadership	4.0	1.0	2	6
Management	4.5	1.0	2	6
Organization	4.0	1.0	2	6
Planning	4.5	1.0	2	6
Problem Solving	4.0	1.0	2	6
Decision Making	4.5	1.0	2	6
Communication	4.0	1.0	2	6
Interpersonal	4.5	1.0	2	6
Group	4.0	1.0	2	6
Team	4.5	1.0	2	6
Leadership	4.0	1.0	2	6
Management	4.5	1.0	2	6
Organization	4.0	1.0	2	6
Planning	4.5	1.0	2	6
Problem Solving	4.0	1.0	2	6
Decision Making	4.5	1.0	2	6
Communication	4.0	1.0	2	6
Interpersonal	4.5	1.0	2	6
Group	4.0	1.0	2	6
Team	4.5	1.0	2	6
Leadership	4.0	1.0	2	6
Management	4.5	1.0	2	6
Organization	4.0	1.0	2	6
Planning	4.5	1.0	2	6
Problem Solving	4.0	1.0	2	6
Decision Making	4.5	1.0	2	6
Communication	4.0	1.0	2	6
Interpersonal	4.5	1.0	2	6
Group	4.0	1.0	2	6
Team	4.5	1.0	2	6
Leadership	4.0	1.0	2	6
Management	4.5	1.0	2	6
Organization	4.0	1.0	2	6
Planning	4.5	1.0	2	6
Problem Solving	4.0	1.0	2	6
Decision Making	4.5	1.0	2	6
Communication	4.0	1.0	2	6
Interpersonal				

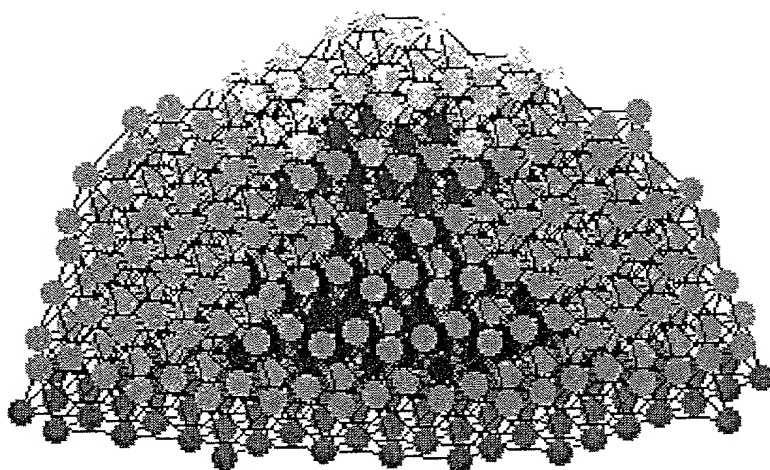


FIG. 4

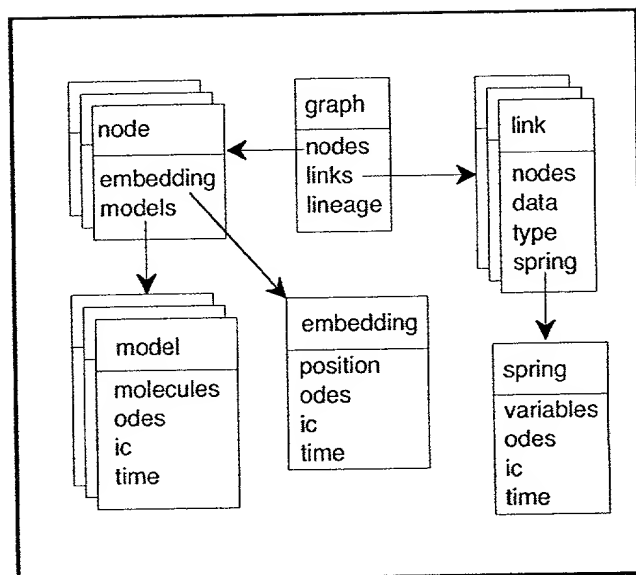


FIG. 5

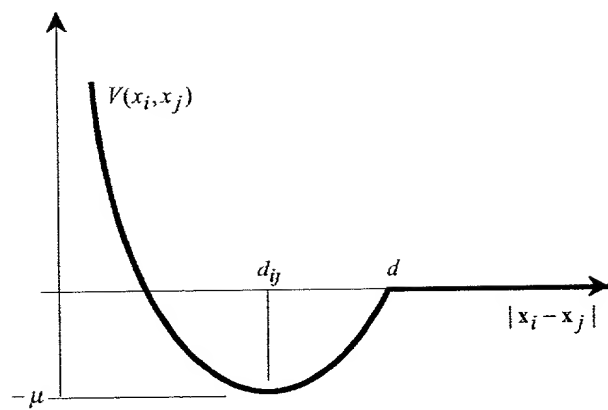


FIG. 6

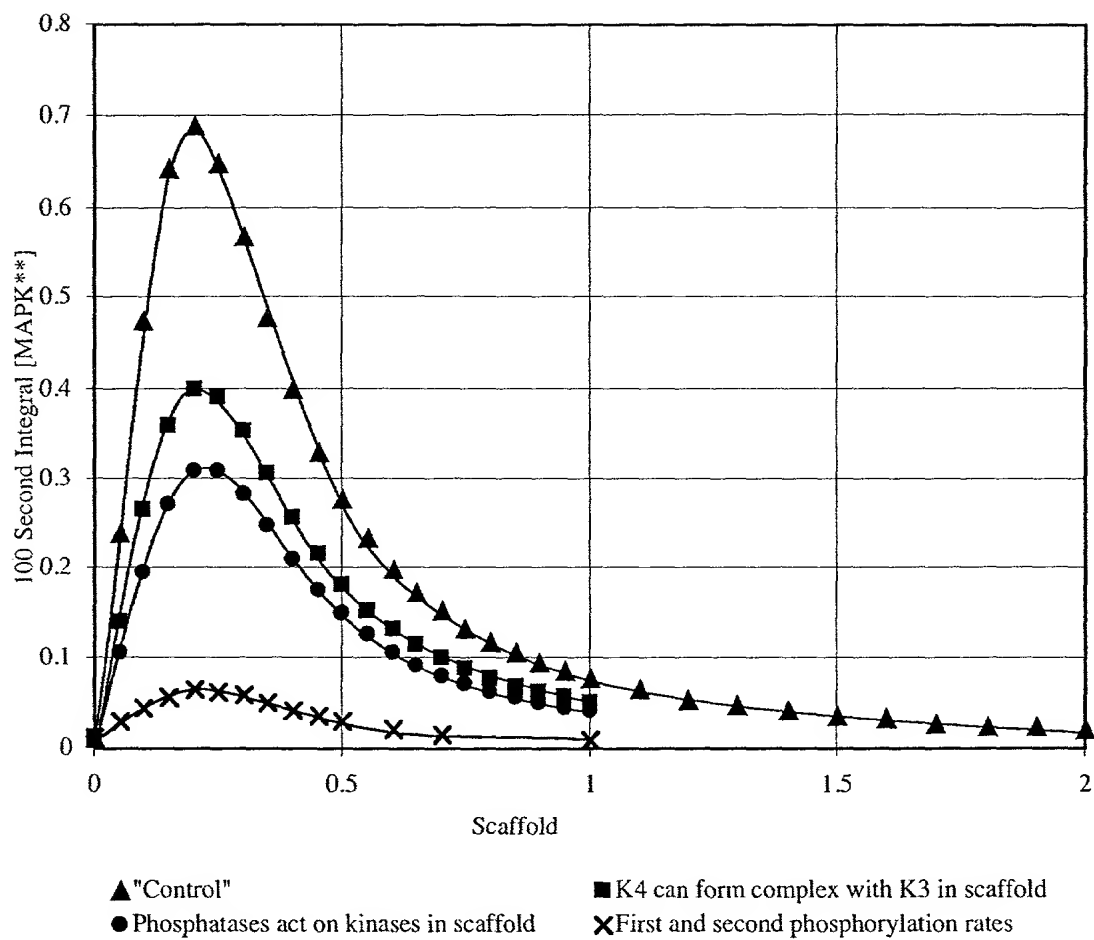


FIG. 7


```
g = unitGraph[odetype → local, threshold → 0.65,
returnPointer → False];
TraditionalForm[g]
```

```
graphDomain[nodes → {nodeDomain[embedding →
embeddingDomain(position → {x(1), y(1), z(1)}, odes → {x(1)'(t) == 0, y(1)'(t) == 0, z(1)'(t) == 0},
ic → {x(1)(0) == 0.114318, y(1)(0) == 0.864451, z(1)(0) == 0.235455}, time → 0)}],
models → {modelDomain[molecules → {c1, M(1), X(1)}, odes →
{c1'(t) == - 0.25 X(1)(t) c1[t] - 0.01 c1[t] + 0.025, M(1)'(t) == - 3 c1[t] (1 - M(1)(t))
- 1.5 M(1)(t) (c1[t] + 0.01), X(1)'(t) == - 0.5 X(1)(t) (c1[t] + 0.3) (1.005 - M(1)(t))
- 0.5 X(1)(t) (1 - X(1)(t)) - 1.005 - X(1)(t) - 0.005}],
ic → {c1[0] == 0.282391, M(1)(0) == 0, X(1)(0) == 0}, time → 0}, modelDomain[molecules →
{splv(1), tspl(1)}, odes → {splv(1)'(t) == θ(M(1)(t) - 0.65), tspl(1)'(t) == θ(splv(1)(t) - 1 × 10-6)},
ic → {splv(1)(0) == 0, tspl(1)(0) == 0}, time → 0}, modelDomain[molecules → {mass(1)},
odes → {mass(1)'(t) == mu mass(1)(t)}, ic → {mass(1)(0) == 1}, time → 0}]]
nodeData → {birth → 0}, nodeType → Cell, links → {}, lineage → tree(1)}
```

FIG. 9

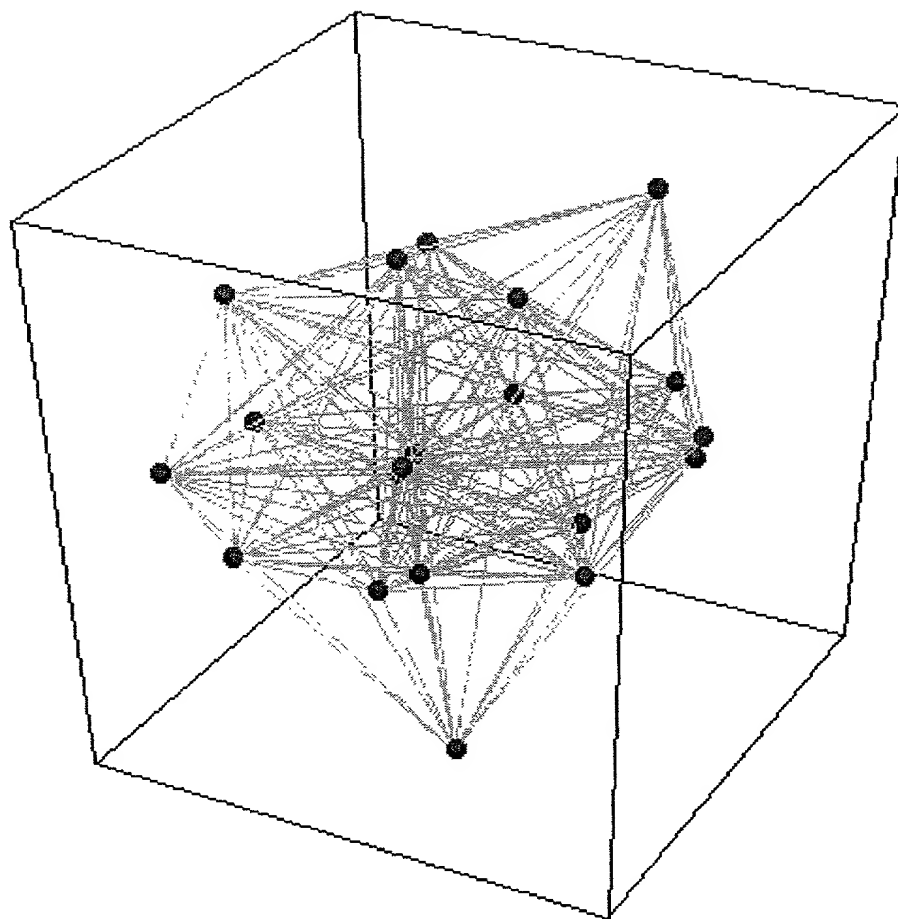


FIG. 10

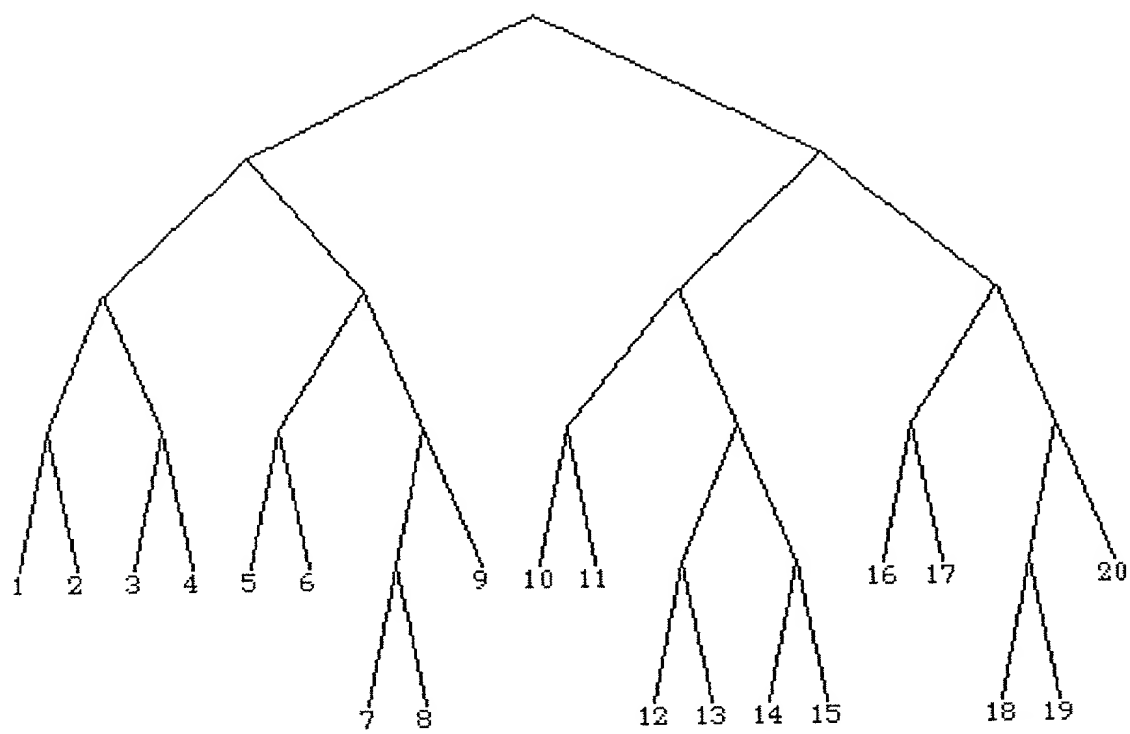


FIG. 11

phosphorylationReactions = genScaffosReacts[S, {2, 2, 1, 1}, K, kphase]

{S[0, 2, -1] → S[1, 2, -1], S[0, 2, 0] → S[1, 2, 0], S[0, 2, 1] → S[1, 2, 1], S[1, 2, -1] → S[2, 2, -1],
 S[1, 2, 0] → S[2, 2, 0], S[1, 2, 1] → S[2, 2, 1], S[-1, 0, 1] → S[-1, 1, 1], S[-1, 1, 1] → S[-1, 2, 1],
 S[0, 0, 1] → S[0, 1, 1], S[0, 1, 1] → S[0, 2, 1], S[1, 0, 1] → S[1, 1, 1], S[1, 1, 1] → S[1, 2, 1],
 S[2, 0, 1] → S[2, 1, 1], S[2, 1, 1] → S[2, 2, 1], S[-1, -1, 0] → S[-1, -1, 1],
 S[-1, 0, 0] → S[-1, 0, 1], S[-1, 1, 0] → S[-1, 1, 1], S[-1, 2, 0] → S[-1, 2, 1],
 S[0, -1, 0] → S[0, -1, 1], S[0, 0, 0] → S[0, 0, 1], S[0, 1, 0] → S[0, 1, 1], S[0, 2, 0] → S[0, 2, 1],
 S[1, -1, 0] → S[1, -1, 1], S[1, 0, 0] → S[1, 0, 1], S[1, 1, 0] → S[1, 1, 1], S[1, 2, 0] → S[1, 2, 1],
 S[2, -1, 0] → S[2, -1, 1], S[2, 0, 0] → S[2, 0, 1], S[2, 1, 0] → S[2, 1, 1], S[2, 2, 0] → S[2, 2, 1]}

FIG. 14

Receive initial condition values, process parameters, and a user representation of the biological network, wherein the user representation is input using one or more of a series of biological network canonical input forms, wherein each canonical input form is based on a type of biological process in the biological network.

10



Generate a series of mathematical equations in an equation output canonical form based on the input representation of the biological network and the process parameters.

20



Numerically solve the series of mathematical equations using the initial condition values and the process parameters, to generate a value or a table of values as a function of time for one or more output functions of the biological network, thereby simulating the biological network.

40

FIG. 15

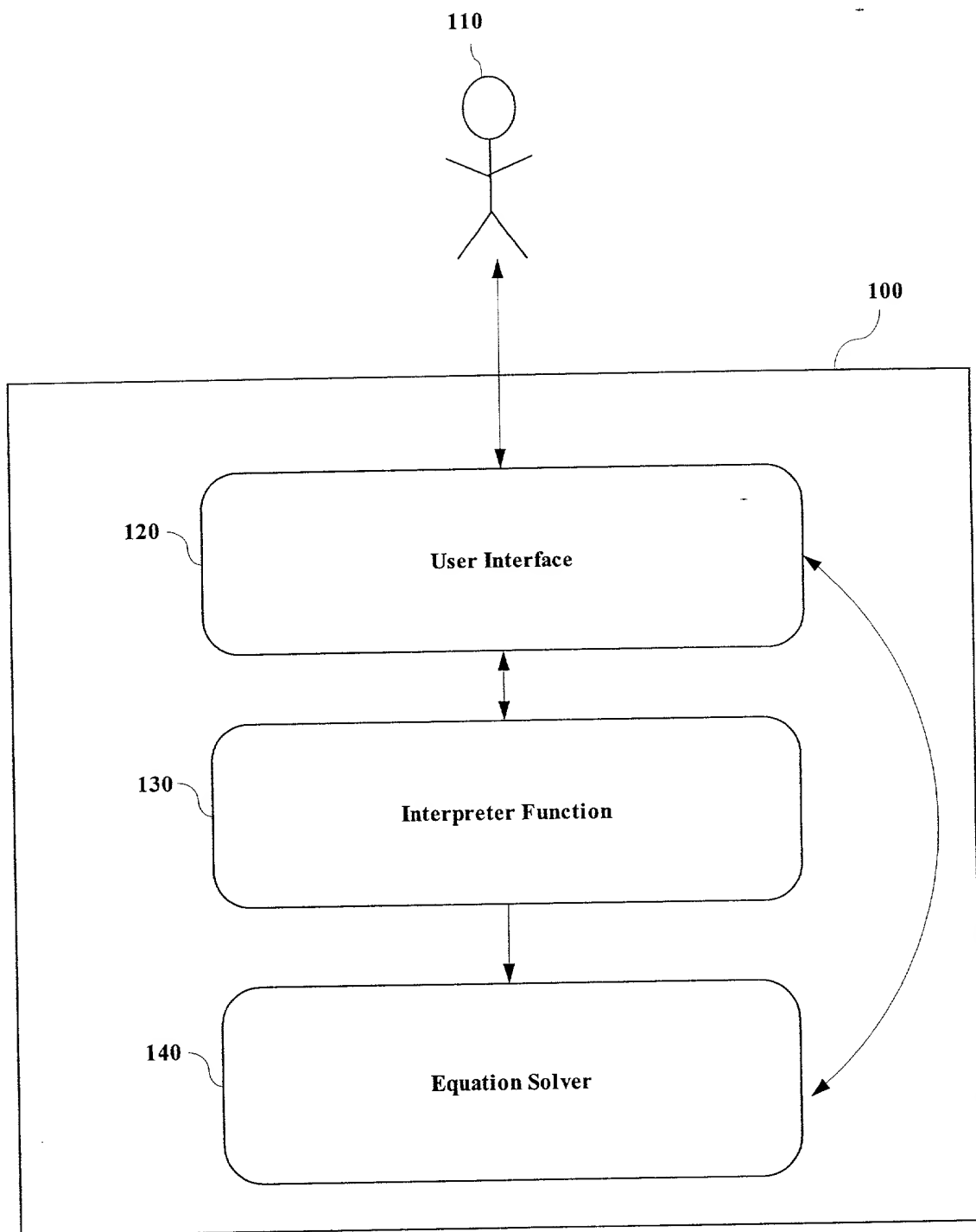


FIG. 16

Out[2]=

```

      RAFFK
{K[3, 0] == K[3, 1], a1, d1, k1, a2, d2, k2},
      RAFF
      K[3, 1]
{K[2, 0] == K[2, 1], a3, d3, k3, a4, d4, k4},
      MEKP
      K[3, 1]
{K[2, 1] == K[2, 2], a5, d5, k5, a6, d6, k6},
      MEKP
      K[2, 2]
{K[1, 0] == K[1, 1], a7, d7, k7, a8, d8, k8},
      MAPKP
      K[2, 2]
{K[1, 1] == K[1, 2], a9, d9, k9, a10, d10, k10},
      MAPKP

```

FIG. 17 (Page 1 of 4)

$\{K[1, 0] + S[-1, -1, -1] \Rightarrow S[0, -1, -1], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, -1, 0] \Rightarrow S[0, -1, 0], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, -1, 1] \Rightarrow S[0, -1, 1], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 0, -1] \Rightarrow S[0, 0, -1], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 0, 0] \Rightarrow S[0, 0, 0], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 0, 1] \Rightarrow S[0, 0, 1], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 1, -1] \Rightarrow S[0, 1, -1], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 1, 0] \Rightarrow S[0, 1, 0], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 1, 1] \Rightarrow S[0, 1, 1], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 2, -1] \Rightarrow S[0, 2, -1], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 2, 0] \Rightarrow S[0, 2, 0], \text{kon, koff}\},$
 $\{K[1, 0] + S[-1, 2, 1] \Rightarrow S[0, 2, 1], \text{kon, koff}\},$
 $\{K[1, 1] + S[-1, -1, -1] \Rightarrow S[1, -1, -1], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, -1, 0] \Rightarrow S[1, -1, 0], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, -1, 1] \Rightarrow S[1, -1, 1], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 0, -1] \Rightarrow S[1, 0, -1], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 0, 0] \Rightarrow S[1, 0, 0], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 0, 1] \Rightarrow S[1, 0, 1], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 1, -1] \Rightarrow S[1, 1, -1], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 1, 0] \Rightarrow S[1, 1, 0], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 1, 1] \Rightarrow S[1, 1, 1], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 2, -1] \Rightarrow S[1, 2, -1], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 2, 0] \Rightarrow S[1, 2, 0], \text{kpon, kpoff}\},$
 $\{K[1, 1] + S[-1, 2, 1] \Rightarrow S[1, 2, 1], \text{kpon, kpoff}\},$
 $\{K[1, 2] + S[-1, -1, -1] \Rightarrow S[2, -1, -1], \text{kpon, kpoff}\},$
 $\{K[1, 2] + S[-1, -1, 0] \Rightarrow S[2, -1, 0], \text{kpon, kpoff}\},$
 $\{K[1, 2] + S[-1, -1, 1] \Rightarrow S[2, -1, 1], \text{kpon, kpoff}\},$
 $\{K[1, 2] + S[-1, 0, -1] \Rightarrow S[2, 0, -1], \text{kpon, kpoff}\},$
 $\{K[1, 2] + S[-1, 0, 0] \Rightarrow S[2, 0, 0], \text{kpon, kpoff}\},$
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 $\{K[1, 2] + S[-1, 1, 1] \Rightarrow S[2, 1, 1], \text{kpon, kpoff}\},$
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 $\{K[1, 2] + S[-1, 2, 0] \Rightarrow S[2, 2, 0], \text{kpon, kpoff}\},$
 $\{K[1, 2] + S[-1, 2, 1] \Rightarrow S[2, 2, 1], \text{kpon, kpoff}\},$
 $\{K[2, 0] + S[-1, -1, -1] \Rightarrow S[-1, 0, -1], \text{kon, koff}\},$
 $\{K[2, 0] + S[-1, -1, 0] \Rightarrow S[-1, 0, 0], \text{kon, koff}\},$
 $\{K[2, 0] + S[-1, -1, 1] \Rightarrow S[-1, 0, 1], \text{kon, koff}\},$
 $\{K[2, 1] + S[-1, -1, -1] \Rightarrow S[-1, 1, -1], \text{kpon, kpoff}\},$
 $\{K[2, 1] + S[-1, -1, 0] \Rightarrow S[-1, 1, 0], \text{kpon, kpoff}\},$
 $\{K[2, 1] + S[-1, -1, 1] \Rightarrow S[-1, 1, 1], \text{kpon, kpoff}\},$
 $\{K[2, 2] + S[-1, -1, -1] \Rightarrow S[-1, 2, -1], \text{kpon, kpoff}\},$
 $\{K[2, 2] + S[-1, -1, 0] \Rightarrow S[-1, 2, 0], \text{kpon, kpoff}\},$
 $\{K[2, 2] + S[-1, -1, 1] \Rightarrow S[-1, 2, 1], \text{kpon, kpoff}\},$
 $\{K[2, 0] + S[0, -1, -1] \Rightarrow S[0, 0, -1], \text{kon, koff}\},$
 $\{K[2, 0] + S[0, -1, 0] \Rightarrow S[0, 0, 0], \text{kon, koff}\},$
 $\{K[2, 0] + S[0, -1, 1] \Rightarrow S[0, 0, 1], \text{kon, koff}\},$
 $\{K[2, 1] + S[0, -1, -1] \Rightarrow S[0, 1, -1], \text{kpon, kpoff}\},$
 $\{K[2, 1] + S[0, -1, 0] \Rightarrow S[0, 1, 0], \text{kpon, kpoff}\},$
 $\{K[2, 1] + S[0, -1, 1] \Rightarrow S[0, 1, 1], \text{kpon, kpoff}\},$
 $\{K[2, 2] + S[0, -1, -1] \Rightarrow S[0, 2, -1], \text{kpon, kpoff}\},$

FIG. 17 (Page 2 of 4)

```

{K[2, 2] + S[0, -1, 0] = S[0, 2, 0], kpon, kpooff},
{K[2, 2] + S[0, -1, 1] = S[0, 2, 1], kpon, kpooff},
{K[2, 0] + S[1, -1, -1] = S[1, 0, -1], kon, koff},
{K[2, 0] + S[1, -1, 0] = S[1, 0, 0], kon, koff},
{K[2, 0] + S[1, -1, 1] = S[1, 0, 1], kon, koff},
{K[2, 1] + S[1, -1, -1] = S[1, 1, -1], kpon, kpooff},
{K[2, 1] + S[1, -1, 0] = S[1, 1, 0], kpon, kpooff},
{K[2, 1] + S[1, -1, 1] = S[1, 1, 1], kpon, kpooff},
{K[2, 2] + S[1, -1, -1] = S[1, 2, -1], kpon, kpooff},
{K[2, 2] + S[1, -1, 0] = S[1, 2, 0], kpon, kpooff},
{K[2, 2] + S[1, -1, 1] = S[1, 2, 1], kpon, kpooff},
{K[2, 0] + S[2, -1, -1] = S[2, 0, -1], kon, koff},
{K[2, 0] + S[2, -1, 0] = S[2, 0, 0], kon, koff},
{K[2, 0] + S[2, -1, 1] = S[2, 0, 1], kon, koff},
{K[2, 1] + S[2, -1, -1] = S[2, 1, -1], kpon, kpooff},
{K[2, 1] + S[2, -1, 0] = S[2, 1, 0], kpon, kpooff},
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{K[2, 2] + S[2, -1, -1] = S[2, 2, -1], kpon, kpooff},
{K[2, 2] + S[2, -1, 0] = S[2, 2, 0], kpon, kpooff},
{K[2, 2] + S[2, -1, 1] = S[2, 2, 1], kpon, kpooff},
{K[3, 0] + S[-1, -1, -1] = S[-1, -1, 0], kon, koff},
{K[3, 1] + S[-1, -1, -1] = S[-1, -1, 1], kpon, kpooff},
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{K[3, 0] + S[0, -1, -1] = S[0, -1, 0], kon, koff},
{K[3, 1] + S[0, -1, -1] = S[0, -1, 1], kpon, kpooff},
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{K[3, 0] + S[0, 1, -1] = S[0, 1, 0], kon, koff},
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{K[3, 0] + S[0, 2, -1] = S[0, 2, 0], kon, koff},
{K[3, 1] + S[0, 2, -1] = S[0, 2, 1], kpon, kpooff},
{K[3, 0] + S[1, -1, -1] = S[1, -1, 0], kon, koff},
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{K[3, 1] + S[1, 0, -1] = S[1, 0, 1], kpon, kpooff},
{K[3, 0] + S[1, 1, -1] = S[1, 1, 0], kon, koff},
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{K[3, 1] + S[1, 2, -1] = S[1, 2, 1], kpon, kpooff},
{K[3, 0] + S[2, -1, -1] = S[2, -1, 0], kon, koff},
{K[3, 1] + S[2, -1, -1] = S[2, -1, 1], kpon, kpooff},
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{K[3, 0] + S[2, 1, -1] = S[2, 1, 0], kon, koff},
{K[3, 1] + S[2, 1, -1] = S[2, 1, 1], kpon, kpooff},
{K[3, 0] + S[2, 2, -1] = S[2, 2, 0], kon, koff},
{K[3, 1] + S[2, 2, -1] = S[2, 2, 1], kpon, kpooff},

```

FIG. 17 (Page 3 of 4)


```

([MAPKP'[t] == -a8 MAPKP[t] K[1, 1][t] -
  a10 MAPKP[t] K[1, 2][t] + d8 K#MAPKP[1, 1][t] + k8 K#MAPKP[1, 1][t] +
  d10 K#MAPKP[1, 2][t] + k10 K#MAPKP[1, 2][t], MEKP'[t] ==
  -a4 MEKP[t] K[2, 1][t] - a6 MEKP[t] K[2, 2][t] + d4 K#MEKP[2, 1][t] +
  k4 K#MEKP[2, 1][t] + d6 K#MEKP[2, 2][t] + k6 K#MEKP[2, 2][t],
  RAFK'[t] == -a1 RAFK[t] K[3, 0][t] + d1 K#RAFK[3, 0][t] +
  k1 K#RAFK[3, 0][t] - k1a RAFK[t] S[-1, -1, 0][t] -

```

FIG. 18 (Page 1 of 10)